



CLEOPATRA'S NEEDLE: THE HISTORY AND LEGACY OF SILICONE INJECTIONS

Citation

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CLEOPATRA'S NEEDLE

THE HISTORY AND LEGACY OF SILICONE INJECTIONS

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JANUARY, 1997

CLEOPATRA'S NEEDLE'

THE HISTORY AND LEGACY OF SILICONE INJECTIONS

I. Silicone fluid: the developmental years (1940-1963)

A. What is silicone?

Scientists and science fictionwriters alike have fantasized that an entire parallel universe could be built on silicone rathe than carbon base.

—Philip Hilts, 1992

Silicone is not a single chemical. Rather, the silicones are a family of chemically related substances all having in common silicon atoms that are bonded to oxygen and carbon atoms.³ Silicone molecules have a backbone of silicon attached to carbon; other organic groups can be bonded to the silicon atom as well. The basic unit composing all silicones is the diorganosiloxy group:

R

-O-Si-C-

R

'Cleopatra's Needle' is a term used to describe the silicone injection of breasts in the buxom belles of Hollywood and Las Vegas. E. Norling, Cleopatra's Needle, Orange County (Cal.) Bulletin, October, 1968

² Philip Hilts, Strange history of silicone held many warning signs, New York Times, Jan. 18, 1992.

Silicone, discussed here, must be distinguished from the atom silicon and the compound silica. The term silicone was coined by Dr. Fredrick Kipping as a contraction between 'ketone and silicon. Silicon is an element not found in a pure form in nature. As a compound with oxygen, silicon comprises 75% of the earth's crust. Isolating pure silicon from its compounded form was first performed in 1824, but did not become commercially practical until the 1930's. The invention of the semiconductor in the early 1940's provided additional economic stimulus for producing silicon more efficiently. (Note that one refers to Silicon Valley, not SilicQn^..Valley when speaking of the computer industry in the Bay Area.) Silicon bonded to two oxygen atoms forms the compound silica. Silica has many commercial uses, including glass, ceramics and industrial dessicants and binders. In its natural form, silica is in a crystalline form thought not to be toxic as a food additive but hazardous when inhaled. Silicosis and lung cancers result from respiratory exposure. Amorphous (non-crystalline) silica lacks the ordered geometry that comprises a crystal. In its amorphous form, silica is thought to be much less pathogenic. Of note, amorphous silica is used as a reinforcing agent in the formation of silicone plastics for medical uses. See R. LeVier, M. Harrison, R. Cook, T. Land, ~'What is silicone, Plast. Reconstr. Surg. 92: 163, 1993.

The most common organic [R] group is the methyl group [-CH₃], although other groups can be used, often in combination with methyl groups. Silicones found in medical applications are thus termed polydimethylsiloxanes.⁴ Silicon, with four chemical valencies, resembles carbon in its versatility.⁵ Described as a wonder substance, silicone could be turned into products that were stronger than plastic, yet more flexible than glass.⁶ A Fortune magazine story in 1947 devoted eight pages to extolling its industrial virtues.⁷

Silicones come in different physical forms, from watery liquids to solid resins.⁸ The physical properties are determined by the length of their molecular chains and by their degree of crosslinking or polymerization. The longer the chain, the higher the viscosity of the substance.⁹ Silicone gel, like the filler in breast implants, is a molecular hybrid, with matrix of long cross-linked molecules and interstitial filler of silicone oil. Levier et al. in 1993 described the gel used in breast implants as a polydimethylsiloxane polymer chemically crosslinked with vinyl bridges to form a polymer network, and polymer chain entanglement adds apparent crosslinks. Cohesive gel is formed when this network is swollen with 1000 cs viscosity polydimethylsiloxane fluid.¹⁰ Silicone is made more solid by increasing the length of the polymer chains and increasing the degree of cross-linking.

~ F. Ashley, S. Braley, T. Rees, D. Goulian and D. Ballantyne, The present status of silicone fluid in soft tissue augmentation, *Plast. Reconstr. Surg.* 39:411, 1967, p. 419. This article also describes how silicone fluid is produced.

See JY. Cory, Historical overview and comparison of silicon with carbon, pp. 1-56 in S. Patai and Z. Rappaport, Eds. The Chemistry of Organic Silicon Compounds (New York: Wiley, 1989).

6 J. A. Byrne, *Infrared Spectroscopy* (New York: McGraw-Hill, 1995), p. 30.

~ The silicones: cornerstone of a new industry, *Fortune* 35:104-111, May, 1947

Silly putty represents a failed attempt to produce a commercially useful silicone rubber.

~ The fluid used for injection under the 1965 IND 2702 had a viscosity of 350 centistokes (with 1 centistoke [cs] equal to the viscosity of water).

10 Levier et al., What is silicone, p. 165, Fig. 1.

Heat vulcanization and room-temperature (catalytic) vulcanization are techniques used in the industry to produce silicone resins and rubbers. The external shell containing silicone gel for breast implants is an example of silicone rubber that has undergone room temperature vulcanization.¹¹

B. Silicone use in industry

Polydimethylsiloxane: the grease that helped win the war.

– Warrick, 1990¹²

Despite the association in the public mind between silicone and cosmetic surgery, the potential medical uses of this chemical did not motivate its development. The story of silicone began in the late 1800's, when F.S. Kipping at Nottingham University introduced a practical method for synthesizing the carbon-silicon bond.¹³ By 1944, he had published 54 papers on the subject pertaining to the chemistry of the substances that could be made with this type of bond. Many of his experiments resulted in what he termed uninviting glues.¹⁴ Commercial exploration had to await the mid-1930's, when Coming Glass Works hired their first organic chemist, Frank Hyde. Working for a glass company required Dr. Hyde to have familiarity with the properties of silicon. When he encountered the research of Prof. Kipping, he realized that many of Kipping's uninviting glues could have useful properties for industrial uses: the silicon backbone of the molecule provided inertness and heat stability, while the organic portion of the molecule would permit

¹¹ This process is described in F. Ashley, S. Braley, T. Rees, D. Goulian and D. Ballantyne, The present status of silicone fluid in soft tissue augmentation, *Plast. Reconstr. Surg.* 39: 411, 1967, p. 4 19-420.

¹² E. L. Warrick, Forty Years of Firsts (New York: McGraw-Hill, 1990), p. 36.

¹³ Starting the story at this time leaves out earlier chemists whose contributions made Kipping's work possible. For an overview of this history, see E. G. Rochow, Introduction to the Chemistry of Silicones (Wiley: New York, 1951). The first organosilicon compound (that is, one with a carbon-silicon bond) was prepared by Friedel and Crafts in 1863, but the commercial production of these compounds had to await the introduction of the Grignard reagent at the turn of the century.

¹⁴ • A. Braley, The use of silicones in plastic surgery: a retrospective view, *Plast. Reconstr. Surg.*

51: 280, 1973.

polymerization. At the same time, R.R. McGregor, a Corning Glass Research Fellow at the Mellon Institute in Pittsburgh, began basic research on these substances.¹⁵

By the early 1940's, these research efforts yielded information about industrial applications for silicone materials. Coming Glass had originally been looking into silicone to provide caulking material for their glass brick products that were popular in the 1930's.¹⁶ Though not a good substitute for mortar, silicone was observed to have rubber-like properties that inspired further research during the rubber shortages in World War II. At the request of Admiral Rickover, Hyde collaborated with Earl Warrick to produce the first polydimethylsiloxane fluid in 1940.¹⁷ However, the small quantities produced by Corning Glass did not satisfy the military's requirements. Since the synthesis of silicones was a matter of organic chemistry rather than glass-making, Corning Glass sought the assistance of Dow Chemical in further product development. Their collaboration resulted in the formation of the corporate joint venture, Dow Coming, in 1943.¹⁸ Early products included silicone fluid for dampening vibrations in Air Force instruments, non-melting grease for insulating military spark plugs, antifoaming agent that prevented bubbles from forming in motor oil at high altitudes, and high-temperature resistant rubbers to dampen vibrations in cooling fins of aircraft motors.¹⁹ One of the first products to reach wide usage was a silicone liquid used to insulate electrical transformers. By the end of World War II, silicone was used for this purpose wherever the US employed electrical transformers.²⁰

¹⁵ R.R. McGregor, Silicones and Their Uses (New York: McGraw-Hill, 1954).

¹⁶ Warrick, Forty Years ..., p. 9-10.

¹⁷ Ibid., p. 26.

¹⁸ Details about the formation of this joint venture are presented in Warrick, Forty Years ..., pp. 43 ff.

¹⁹ Braley, The use of silicones..., p. 281. Also see Warrick, Forty Years ..., p. 36.

²⁰ P.J. Hilts, Strange history of silicone ... ; also J. Foreman, Women and silicone: a history of risk , Boston Globe, January 19, 1992, Sunday, City Edition.

C. Early medical uses for silicone

Since the silicones are relatively new, having been in existence only for the past 20 years, there is much uncertainty and lack of knowledge in the profession relative to them

– Blocksma and Braley, 1965²¹

At the end of World War II, when the military contracts expired, silicone was a product without a market.²² McGregor and his colleagues at Dow-Corning therefore investigated various commercial uses, including furniture polish, high temperature paints, insulation, caulking and waterproofing.²³ Medical applications for silicone were also developed, both orthodox and unorthodox. One notable use became evident when American Army quartermasters noticed drums of transformer insulating fluid began disappearing from the docks of Yokohama Harbor in Japan. This material was injected into the breasts of Asian prostitutes who sought a more Western appearance to cater to the American servicemen.²⁴ The popularity of these techniques spread throughout eastern Asia as silicone injections in the breast were thought to avoid the known perils of other techniques.²⁵

²⁰ R. Blocksma and S. Braley, The silicones in plastic surgery, *Plast. Reconstr. Surg.* 35:366, 1965.

²² Warrick, *Forty Years* p. 86 ff.

²³ McGregor, *The Silicones*

²⁴ Hiltz, *ibid.*, and Foreman, *ibid.* Their reports correspond with the history told me by my father, a medical officer in Japan at that time, who knew personally an army master sergeant who administered breast injections to local women for a fee. The sergeant apparently obtained the syringes illicitly from the military medical facilities and used what my father described as cooling fluid readily available on the base. This behavior did not bring about any official censure. My father did not know the chemical make-up of the cooling fluid. (Personal communication, Charles R. Webb, M.D., 1990) Even if the fluid were not silicone, this history suggests that the technique of breast injection with military chemicals was familiar to some army personnel of that time.

Complications from some of these other techniques, such as paraffin injections and petrolatum (Vaseline) injections, were described by one author as hair-raising. F. Ortiz-Monasterio and I. Trigos, Management of patients with complications from injections of foreign materials into the breasts, *Plast. Reconstr. Surg.* 50:42, 1972.

In addition to this illicit use of industrial silicone, a variety of innovative therapeutic uses were investigated for this product. Since silicone could be applied to glass to prevent liquids from adhering, the substance was used to coat penicillin bottles and blood-handling glassware.²⁶ Silicone rubber was used to form an artificial urethra implanted in a patient whose own tissues had been destroyed by venereal disease; this device was successful at 14 months follow-up.²⁷ Silicone sponges were used to fill thoracic cavities left after surgical treatment of pulmonary tuberculosis, with minimal local reaction.²⁸ When a surgeon at the University of Michigan sought to develop an artificial bile duct, Dow fabricated its first silicone rubber for medical use, Silastic~ S-9711 and its extrudable counterpart, Silastic~ S~2000.²⁹ In 1955, the first successful shunt was placed to drain excess cerebrospinal fluid into the heart in pediatric hydrocephalus.³⁰

Plastic surgeons were also realizing the potential of silicone products. Dr. James Barrett Brown first became aware of these substances in 1947. Although the use of silicone for burn patients was Brown's initial concern, he also noted that the substance could help solve the age-old problem of soft tissue supplementation.³¹ Restoring contour to parts of

²⁶ L. Jaques, E. Fidler, E. Feldstein, A. MacDonald, Silicones and blood coagulation, *Canad. Med. Assoc. J.* 55:26, 1946.

²⁷ R. De Nicola, Permanent artificial (silicone) urethra, *J. Urol.* 63:168, 1950. Silicone rubber is commonly used for urological products such as catheters to the present day.

²⁸ J. Gale, A. Curreri, W. Young, H. Dickie, Plastic sponge prosthesis following resection in pulmonary tuberculosis, *J. Thorac. Surg.* 24:587, 1952. See also J. Frindlay and O. Clagett, A plastic sponge prosthesis for use after pneumonectomy: a preliminary report of an experimental study, *Mayo Clin. Proc.* 24: 538, 1949.

²⁹ Braley, *Silicones ...*, p. 282. The surgeon, Dr. Roger Murray, was unable to produce a leak-proof anastomosis between the artificial material and the living tissue, so the artificial bile duct experiment failed.

³⁰ The shunt was devised by John Holter, an engineer whose baby was born with hydrocephalus. Holter had invented a stainless steel valve that could be connected to tubing allowing one-way drainage of cerebrospinal fluid into the heart. He contacted Dow Corning for the requisite tubing. Warrick states that over the next 10 years, over 600,000 such shunts, using Silasticml tubing had been implanted. See Warrick, *Forty Years...*, p. 185.

³¹ J. Barrett Brown, M. Fryer, P. Randall, M. Lu, Silicones in plastic surgery: laboratory and clinical investigations, a preliminary report, *Plast. Reconstr. Surg.* 12: 374, 1953.

the body that had been damaged or congenitally deformed was, then as now, a fundamental part of plastic surgery. Lack of a good substitute for missing tissue had bedeviled both cosmetic and reconstructive practitioners from the earliest times, especially when a large volume of filler was necessary. Skin grafting was well-established for resurfacing a denuded area, but filling out a contour defect posed a more difficult problem. Potential applications for alloplastic materials envisioned by surgical innovators seemed tailor-made for various silicone products. Hard silicone plastic could be used in cosmetic surgery to augment cheeks, chins and noses. Rubbery silicone could be used as penile implants, silicone bags containing silicone gel could enlarge breasts or replace surgically-removed testicles. Silicone injections offered particular promise for small contour deficiencies like scars and wrinkles, where the placement of the material subcutaneously would plump out a depressed area.³² Larger doses of silicone injections were envisioned for major volume restoration, whether for the breast, the body or the face.

Brown et al. 's paper anticipated some of these applications. Though it added little real information to what was already known about silicone, it was the first published paper on the subject in the plastic surgery literature.³³ Silicone was considered for medical use both in its fluid form for injection and in its rubber or hard resin form. At about the same time, Scales published his criteria for the ideal soft tissue substitute.³⁴ The apparent conformity of silicone with these criteria was apparent to plastic surgeons and Dow alike.

³² E. Wegener, The problem of correction of forehead wrinkles, *Med. Kosmetik.*, 5:136, 1957.

³³ Only fairly recently, though, has there been a generally accessible plastic surgery literature in the United States. Plastic and Reconstructive Surgery, the leading journal in the field, was founded in 1946. The American Board of Plastic Surgery was established in 1937. Much of the innovation in the field between

the World Wars took place in Europe, both in Britain and on the Continent. See J. McCarthy, Introduction to plastic surgery, pp. 1-24 in J. McCarthy, Ed. *Plastic Surgery*. V. I (Philadelphia: W.B. Saunders Co., 1990) for a historic overview of the specialty. It is likely that the political unrest in the late 1930's in Europe and the economic distress in the United States had an impact upon the development of the specialty as a cohesive field with a well-established scientific methodology.

³⁴ J.T. Scales. Discourse on metals and synthetic materials in relation to soft tissues; tissue reaction to synthetic materials, *Proc. Roy. Soc. Med.*, 46:647, 1953.

Silicone was considered, in keeping with Scales' criteria, to be 1) not physically modified by soft tissue, 2) chemically inert, 3) not inducing inflammation or foreign body reaction, 4) noncarcinogenic, 5) producing no allergy or hypersensitivity, 6) capable of resisting mechanical strains, 7) capable of fabrication in the form desired and 8) sterilizable. Despite these appealing characteristics, the plastic surgery literature contains only a few reports of research on silicone materials during the years following Barrett-Brown et al.'s paper.³⁶

Toxicological research was being conducted independently, without reference to specific clinical uses for silicone. The first studies on silicone fluids in animals determined that the substances had low toxicity even at high doses.³⁷ These same studies quoted in a clinical article were said to demonstrate that silicone is practically inert physiologically and non-toxic to body tissues.³⁸ Oral administration failed to cause discernible effects.³⁹ Though all research at the time agreed that silicone fluid was non-toxic whether ingested orally, or injected subcutaneously, intraperitoneally or intravascularly, there was evidence after administration by the intraperitoneal or intravascular routes that the substance was found in tissues distant from the site of administration.⁴⁰ Local reactions to silicone were evaluated in the same studies. Inflammatory reactions were described to different extents, depending upon the dose and route of silicone administration. Silicone fluid was known to

~ R. Blocksma and S. Braley, The silicones in plastic surgery, *Plast. Reconstr. Surg.* 35:366, 1965.

³⁶ I have not been able to identify a historic reason for this dearth of published research.

~ V. K. Rowe, H. Spencer and S. Bass, Toxicological studies on certain commercial silicones and hydrolyzable silane intermediates, *J. Industrial Hygiene and Toxicology*, 30: 332, 1948.

~ R. Barondes, W. Judge, C. Towne and M. Baxter, The silicones in medicine: new organic derivatives and some of their unique properties, *Mil. Surgeon* 106:379, 1950.

~ V. K. Rowe, H. Spencer, S. Bass, Toxicological studies on certain commercial silicones II. Two year dietary feeding of DC Antifoam A to rats, *Arch. Industr Hyg.* 1:539, 1950.

~ e Rowe et al., Toxicological studies ... [I and II].; Barondes et al., *ibid*; S. Kern and R. Anderson, Observations on the toxicity of methyl-silicone, *J. Am. Pharm. Association* 38:575, 1949.

produce different reactions than silicone rubber, but in both cases local reactions were deemed slight.⁴¹

These studies were flawed from the perspective of modern research: the data were poorly tabulated, the fate of each animal could not be followed throughout the protocol, and the length of follow-up was inadequate for determination of anything but acute or subacute toxicity. Though Dow Corning claimed to have carried out life-cycle observations in 245 animals over 12 years by 1960, Brown, et al. commented that this data was inadequate.⁴² Despite the limitations of this research, clinicians relied on it uncritically well into the 1960's.

In part, these limitations bespeak the corporate culture at Dow Corning in the 1950's. Its major focus was on industrial uses for silicone products, with medical applications considered an insignificant part. In these early years of product development, Dow Corning had neither the research interest nor the facilities to carry out what we today would consider appropriate testing for medical products. A more free-wheeling attitude prevailed. Simon Braley, a personable chemist at Dow-Corning who became intimately involved in the promotion of biological applications for silicone⁴³, described without apparent misgiving the response of Dow to medical innovators who sought information about the product:

Since our knowledge of the physiological responses of the silicones at that time was limited ... and because our medical training was so scanty as to make most of the questions incomprehensible to us, we found ourselves at a loss... However, since the silicone industry had for years manufactured materials that were looking for applications, and because our scientific curiosity was piqued, we endeavored to answer as best we could – although our answer was usually some variant of I

⁴¹ F. Marzoni, S. Upchurch, C. Lambert, An experimental study of silicone as a soft tissue substitute, *Plast. Reconstr. Surg.* 24:600, 1959.

⁴² J. B. Brown, M. Fryer and D. Ohlwiler, Studies and use of synthetic materials such as silicone and teflon as subcutaneous prostheses, *Plast. Reconstr. Surg.* 26:263, 1960.

⁴³ Silas Braley is described at some length in Byrne, Informed Consent, p.139 ff.

don't know, doctor. Here is a sample. Try it in your animals and see what happens.

D. Silicone injections and the breast

Silicone injections were one of the first successful Japanese exports into America.

– J. Byrne, 1995 ~ ~

The quest for ideal soft tissue replacement or supplement has for decades focused on the female breast. Soft tissue inadequacy (small or ptotic breasts) has led to women seeking both natural and artificial means of breast augmentation. Mammoplasty procedures, eulogized by surgeons, have not always produced the same degree of enthusiasm among patients. Silicone breast implants have been decried by Esther Rome as a great experiment upon women.⁴⁷ Prior to the development of silicone breast implants, however, other experiments with alloplastic materials were conducted whose outcomes were so dismal that silicone gel implants were viewed as a marked advance in women's health. Among these experiments was the injection of silicone fluid.

Braley, *Silicones ...*, p. 282.

~ Byrne, *Informed Consent*, p. 41.

⁴⁶ See, for example, J. Lalardrie and R. Mouly, History of mammoplasty, *Aesth. Plast. Surg* 2:167-176, 1978, for a particularly poetic rhapsody about cosmetic breast surgery.

~ Quoted in P. Corrigan, Breast implants ... FDA order sparks debate on safety, *St. Louis Post-Dispatch*, June 2, 1991, p. 1A.

~ The Ivalon (polyvinyl alcohol) sponge, devised in 1949, is described in W. Pangman and R. Wallace, The use of plastic prosthesis in breast plastic and other soft tissue surgery, *West. J. Surg.* 65:503, 1955; the Polistan (polyethylene) sponge, formulated in 1950, was described in Z. Neuman, The use of the non-absorbable polyethylene sponge 'polystan sponge' as a subcutaneous prosthesis, *Br. J. Plast. Surg* 9:195, 1957; Etheron (polymethene), introduced in 1960, was reported in P. Regnault, One hundred cases of retromammary implantation of etheron, followed up for thirty months, *Transactions of the Third International Congress of Plastic and Reconstructive Surgery* (Amsterdam: Excerpta Medica, 1964), pp. 78-

80.

Earliest use of silicone fluid for breast augmentation remains undocumented in the Western medical literature.⁴⁹ This may reflect the fact that these procedures were not being performed under medical supervision, so might not at first have been the subject of clinical observation. American physicians became aware of the technique as Asian patients arrived in the United States in the 1950's. Still, the use of silicone for breast augmentation remained a black-market type of procedure, carried out by cosmeticians or injection specialists to cater to the demands of women in the entertainment industry.⁵⁰ The source of this fluid was the only commercial producer, Dow Corning. During this time period, though, the company had not directed any of its research efforts towards developing a purified silicone oil strictly for medical purposes.⁵¹ Even with the establishment of the Dow Center for Aid to Medical Research in 1959, purification of Dow Corning 200 fluid was not undertaken. Silicone injections in the 1950's and early 1960's still involved transformer fluid.

The procedure began to attain some notoriety by the early 1960's. A doctor in Las Vegas was quoted in a 1963 Newsweek article as having injected 200 women with a total of 16,000 doses of silicone.⁵² Carol Doda in 1964 transformed herself from a 38-C to a 40-DD through a series of silicone injections, assuring her place in history as an icon in topless dancing. As the procedure gained popularity, reports of complications emerged,

~ Even in the Japanese literature, the first report of silicone injections in a plastic surgery journal was not published until 1961. J. Uchida, Clinical applications of cross-linked dimethylpolysiloxane; restoration of breast, cheeks, atrophy of infantile paralysis, funnel-shaped chest, etc., Jap. J. Plast. Reconstr. Surg.

4:303, 1961.

~ Foreman. Women and silicone

~ Warrick, *Forty Years* ... p. 169 ff.

³² Newsweek, Escalation, 10/25/63, p.¹ 10. Norman Anderson, in his 12/18/90 testimony, described some 50,000 women in the U.S. who had been injected with silicone. Cf. Hearings before the Human Resources and Intergovernmental Relations Subcommittee of the Committee on Government Operations, December 18, 1990, p. 30.

first episodically and then more systematically.⁵³ In the 1960's, for example, a 40 year-old woman died after breast injections when some of the silicone fluid traveled to her lungs.⁵⁴ A Ms. Magazine article described a woman's experiences with breast injections as a teenager in the 1960's, a series of procedures that ultimately left both breasts painful, lumpy, and rock-hard, with collapsed nipples and silicone cysts requiring needle aspiration.⁵⁵ Clinicians seeing large numbers of women with silicone injected into their breasts were reporting similar complications.⁵⁶

Complications like lump formation, firmness and tenderness are understandable physiologically when one considers how the body reacts to silicone injections. Injected in a relatively pure form, silicone fluid nonetheless elicits a local inflammatory reaction and stimulated scar tissue formation as the body endeavored to wall off the foreign substance. The silicone oil has the tendency to break up into progressively smaller droplets following injection, with each droplet eliciting its own process of scar tissue formation. This process was described in a case report where a large volume of silicone fluid had been injected for breast enlargement:

The histological slides demonstrate vacuoles previously filled with silicone of diameters varying in size from 1/100 of a millimeter to one millimeter, and the gross inspection of the removed specimen showed cysts varying in size from 1 millimeter to 20 millimeters. If one estimates the total volume of

silicone injected in this case at 555 cc., and the majority of its deposit showing a diameter of 1/10 of a millimeter, one can come to the mathematical conclusion that the foreign body injected remains in the tissue in the form of 30 billion small globules.⁵⁷

~ W. Synimers, Silicone mastitis in topless waitresses. Br. Med. J. 3:19, 1968

~ Byrne, Informed Consent. p. 43. He refers to horror stories that abounded, p. 42.

~ D. Lamed, A shot or two or three in the breast, Ms. September, 1977, p. 55.

⁵⁶ See Khoo Boo-Chai, The complications of augmentation mammoplasty by silicone injection, Br. J. Plast. Surg. 27:28 1, 1968. See also F. Ortiz-Monasteio and I. Trigos, Management of patients with complications from injection of foreign materials into their breasts, Plast. Reconstr. Surg. 50:42, 1965.

~ R. Kaden. Use of silicone oil in cosmetic dermatology, Aesth. medizin. 17:217, 1968, translated from the German.

Each of these foreign bodies can produce its own foreign body reaction, a complicated process involving both scar tissue deposition and cellular response. Vigorous reactions to foreign bodies form tissue masses called granulomata, combinations of scar and cells that work together to isolate and ingest the foreign matter. Granuloma formation has been consistently described in response to silicone injection.⁵⁸ Certain cells found in the inflammatory reactions to silicone injections are potentially immunologically active, while others have the known ability to migrate to other parts of the body after having ingested microscopic amounts of silicone.⁵⁹

As more experience accumulated with silicone injections, it was observed that the fluid had a tendency to displace from the breast area where it had been deposited and migrate to adjacent areas, showing up as irregular subcutaneous masses.⁶⁰ To solve this problem, agents known to create local inflammation were added to the silicone fluid to incite scarring around the injection area so that the fluid would be immobilized in the desired region⁶¹ One version of this formula was popularized by Dr. Sakurai, a Japanese doctor who moved to Beverly Hills and helped popularize the technique.⁶² Dr. Thomas Sternberg, during the discussion of his paper on silicone injections at the 84th Annual Meeting of the American Dermatological Association, remarked that the Sakurai formula had been given to tens of thousands of women by 1964 for wrinkle eradication and breast

~ N. Ben-Hur, D. Ballantyne, T. Rees, Local and systemic effects of dimethylpolysiloxane fluid in mice, *Plast. Reconstr. Surg.* 39:423, 1967.

~ J. Andrews, Cellular behavior in response to injected silicone fluid: a preliminary report, *Plast. Reconstr. Surg.* 38:581, 1966.

~ T. Sternberg, F. Ashley, L. Winer, Tissue reactions to injectable silicone liquids, *Hautartz (Berlin)* 14:281, 1964.

⁶¹ These additives, including vegetable oils and mineral oils, were described by Dr. Norman Anderson, Hearings before the Human Resources and Intergovernmental Relations Subcommittee of the Committee on Government Operations, December 18, 1990, p. 30.

⁶² This formula, its variants and its local effects were described in F. Ortiz-Monasteio and I. Triglos, Management of patients with complications from injection of foreign materials into their breasts, *Plast. Reconstr. Surg.* 50:42, 1972.

enlargement.⁶³ Dr. Harry Kagan, an osteopath who was not a board-certified plastic surgeon, claimed impressive success and minimal complications with his version of the Sakurai formula.⁶⁴ He has been described as an apostle of silicone injections.⁶⁵

Understandably, the adulterants led to problems of their own. Dow Corning claimed, and many clinicians believed, that the problems observed after silicone injections were due to impurities in the injection fluid itself.⁶⁶ To obviate the problem of local tissue reactions, Dow Corning first introduced Medical Fluid 360, and later replaced it with highly purified Medical Grade Fluid MDX 44011 for use in clinical experimentation.⁶⁷ In their series of 186 patients, Ortiz-Monasterio and Trigos emphasized the role that adulterants played in local reactions, concluding that there was no satisfactory solution to some of these problems.⁶⁸

From a contemporary perspective, it seems ironic that the silicone gel breast prosthesis was viewed as a startling advance in women's health. The gel-filled breast implant, though, was initially thought to avoid the conspicuous problems of silicone fluid injections. Early series of case reports seemed to corroborate this impression.⁶⁹ Even as alternative methods of breast enlargement became more available and successful, still a market for silicone injections. An ethical physician might ask, as did Dr. Norling in 1968,

⁶³ Discussion of Tissue reactions to injected silicone liquids, *Arch. Derm.* 91:177, 1965.

~ H. Kagan, Sakurai injectable silicone formula, *Arch. Otolaryngol.* 78:663, 1963. ⁶⁵ Byrne, Informed Consent. p. 43.

⁶⁶ R. Blocksma and S. Braley, The silicones in plastic surgery, *Plast. Reconstr. Surg.* 35:367, 1965.

⁶⁷ F. McDowell, Editorial: complications with silicones – what grade of silicone? how do we know it was silicone? *Plast. Reconstr. Surg.* 61:892, 1978.

⁶⁸ Ortiz-Monasterio and Trigos, Management of patients..., p. 46.

⁶⁹ See, for example, J. Williams, Experiences with a large series of Silastic breast implants, *Plast. Reconstr. Surg.* 49:253, 1972. M. McGrath and B. Burkhardt, The safety and efficacy of breast implants for augmentation mammoplasty, *Plast. Reconstr. Surg.* 74:550, 1984, offers a bibliographic overview of some of these studies.

why silicone injections continue to be used for breast enlargement. He answered his own question: The fees for a series of silicone injections into a patient's breasts are generally greater than those charged ... for insertion of the ... Silastic Mammary Prosthesis.⁷⁰

II. Silicone fluid: years of regulation (1963-1976)

A. Silicone becomes a drug

The use of silicones in medical applications is a happy example of the medical and industrial fraternities working together to adopt an industrial synthetic product to the needs of the patient.

— S. Braley, 1973⁷¹

Dow Corning has claimed that it first became aware of the practices of silicone injection in 1963, when Dr. Harvey Kagan presented his clinical experiences with Dow Corning 200 fluid at a plastic surgery meeting. Kagan described using the non-sterile industrial grade fluid since 1946 on an experimental basis, and pronounced his experiments successful.⁷² He injected as much as 2 liters into patients as part of his clinical experimentation, reporting no systemic reaction or toxicity as a result.⁷³ Other workers were more cautious: Dr. Tom Cronin, for example, stated that [w]e regard injectable fluid silicone as still a highly experimental technique and we cannot recommend its use.⁷⁴

⁷⁰ E. Norling, Cleopatra's needle.

⁷¹ S. Braley, The use of silicones ..., p. 288.

⁷² Byrne, Informed Consent, p. 53.

~ H. D. Kagan, Sakurai injectable silicone formula.

~ T. Cronin, quoted in L. Winer, T. Sternberg and F. Ashley, Tissue reactions to injectable silicone liquids: a report of three cases, Arch. Derm. 90:588, 1964, p. 593. Note that Dr. Cronin was one of the originators of silicone gel breast implants, arguably a competitive product; one could also argue, though, that concerns about the safety of silicone injections inspired Dr. Cronin's search for a viable clinical alternative.

Injection of silicone fluid was a minor concern to Dow Corning prior to this time, as other medical applications appeared more promising. Silicone seemed to be useful, for example, for coating needles, syringes and other tubes for medication delivery to prevent loss of pharmacologically active agents through adsorption. The product available for these uses was the same material that insulated transformers: Dow Corning 200 fluid. When this product was proposed for immersion therapy in burn care, Dow began to consider purifying the substance for direct human contact.⁷⁵ This purified product, Medical Grade 360, was marketed as an alternative to Dow Corning 200 for clinical uses. ⁷⁶ By 1965, the company and the plastic surgery profession were insisting: We cannot overemphasize:

*only properly prepared medical grade silicones should be used for medical applications.*⁷⁷

The development of medical grade silicone corresponded with Dow's awareness that silicone fluid was being used as a drug. Recognizing the market potential for specifically medical uses for silicone, Dow Corning established its Medical Products Division in 1962 and built a special plant for drug manufacture in accordance with the Food, Drug and Cosmetic Act (Tit. 21 §360, U.S.C.A.).⁷⁸ This factory mainly produced silicone rubber products under the trade name SilasticTM.

From this point forward, the FDA was involved in the oversight of Dow Corning's Medical Products Division. Understandably, then, the company met with alarm the 1963

- F. Gerow et al., Silicone immersion treatment of the severely burned patient, p. 146 in Trans. Third Internat. Cong. Plast. Reconstr. Surg. (Amsterdam: Excerpta Medica Foundation, 1964). Dr. Gerow had been Dr. Cronin's resident in Texas in 1959 where the two collaborated to produce a silicone gel breast implant. The initial clinical use of this device was described by Cronin and Gerow at the same meeting. See T. Cronin and F. Gerow, Augmentation mammoplasty: a new 'natural feel' prosthesis, Trans. Third Internat. Cong. Plast. Reconstr. Surg. (Amsterdam: Excerpta Medica, 1964), p. 41. Gerow's initial contact with Dow Corning was in Feb. 1961, when he visited the company to discuss with them his and Dr. Cronin's ideas for breast augmentation. See Braley, The use of silicones ..., pp. 284-5.

⁷⁶ This was noted to be similar chemically to Dow Coming 200 fluid but purified. F. Ashley et al., The present status ..., p. 419.

⁷⁷ Blocksma and Braley, The silicones ... p. 368. Italics in the original.

⁷⁸ Braley, The use of silicones ..., p. 284.

report by Dr. Kagan that he had used Dow Corning 200 Fluid for injections.⁷⁹ Eager to avoid misuse of the Medical 360 fluid, the company required purchasers to sign an affidavit that the material would be used only for lubrication purposes. The product nonetheless came to the notice of the FDA. In 1964, the FDA declared that the Medical 360 fluid would be considered a new drug that therefore would require formal approval.⁸⁰

B. Dow Corning prepares for the FDA

The clinical use of silicone liquids in man [sic] preceded any responsible and controlled experiments in animals.

—Ashley, Braley, Rees, Goulian and Ballantyne, 196781

Dow Corning responded to the FDA's classification by assembling a panel of seven experts to evaluate the pre-clinical data substantiating the safety and efficacy of silicone injections.⁸² Since animal data was sparse, panel members Ashley, Rees and Goulian conducted studies in their own laboratories, involving by their description some 1000 animals.⁸³ The results of the committee's investigation convinced them that silicone fluid was safe for medical use: It was the opinion of this Committee tht the results obtained prior to the FDA ruling [that silicone fluid was a drug] indicated their value and that further

~ Byrne, Informed Consent, p. 43.

~ M. Lappe, testimony at Hearings before the Human Resources and Intergovernmental Relations Subcommittee of the Committee on Government Operations, June 11, 1991 (hereinafter Hearings), pp. 52 ff.

⁸¹ Ashley et al., The present status ... op. cit.

⁸² 5~ Braley, The status of injectable silicone fluid for soft tissue augmentation, *Plast. Reconstr. Surg.* 47:343, 1971.

⁸³ In addition to the references cited in footnotes 38 & 39, the committee relied on Dow Coming data and other published reports, as well as its own members' research. See, for example, R.R. McGregor, Toxicology of certain silicone fluids, *Bull. Dow Corning Center* 2:15, 1960; P. Grasso, L. Golberg and F. Fairweather, An injection of silicones in mice, *Lancet* 2:96, 1964. See also T. Rees, J. Platt, and D. Ballantyne. An investigation of cutaneous response to dimethylpolysiloxane (silicone liquid) in animals and humans. A preliminary report. *Plast. Reconstr. Surg.* 35:131, 1965.

investigations should be conducted.⁸⁴ Further, the committee members perceived a variety of clinical applications where they deemed the product effective in treating a variety of contour deficits.⁸⁵ Ashley et al. had found their experimental work in animals so encouraging that they treated 11 patients with medical grade 360 fluid and reported their findings at the 1964 meeting of the American Society of Plastic and Reconstructive Surgeons.⁸⁶

Despite the committee's enthusiasm for the product, problems were apparent in the animal data prior to the granting of the ND. Methodological flaws in the design of animal studies compromised the collection of scientifically valid data. Careful examination of these papers indicate a lack of information, in animals or in humans, about the fate of injected silicone and the body's long-term reaction to it. As Ashley et al. acknowledged, [i]t has been found that silicone fluid tends to disappear from the injection site, especially when large quantities are injected. Low viscosity fluids may disappear almost entirely.⁸⁷ No one could state with confidence where the fluid went.

Furthermore, the data that were available raised more questions about injected silicone's safety than they answered. Local reactions to silicone injections were observed histologically: there were inflammatory changes and granuloma formation.⁸⁸ Concerns were raised about potential for soft tissue carcinogenesis.⁸⁹ Macrophages, wandering immunologically competent cells that ingest foreign substances, were noted to have

~ F. Ashley, et al., *The present status ...*, p. 411.

⁸⁵ These are summarized in F. Ashley, et al, *The present status ...*, *ibid.* See also F. Ashley, T. Rees,

D. Ballantyne et al., An injection technique for the treatment of facial hemiatrophy, *Plast. Reconstr. Surg.* 35:640, 1965.

⁸⁶ F. Ashley, *The present status ...*, *ibid.* This clinical use of silicone fluid was illegal.

⁸⁷ F. Ashley et al., *The present status ...*, p. 413.

⁸⁸ L. Winer, et al., *Tissue reactions ...*

⁸⁹ N. Ben-Hur and Z. Neuman, Malignant tumor formation following subcutaneous injection of silicone fluid in white mice, *Isr. Med. J.* 22:15, 1963.

intracellular silicone.⁹⁰ Macrophages containing silicone were found regularly in the regional lymph nodes and reticuloendothelial system.⁹¹ Though published reports did not reach the medical literature until the mid- 1960's or later, the findings in these articles emanated from research carried out in the early part of the decade.⁹² It is reasonable to surmise that much of this information was available to Dow Corning's advisory committee.

As early as 1960, serious questions were also raised about the reactions of human tissues to injected silicone. James Barrett Brown, an early investigator in the medical uses of silicone, commented with co-workers that clinical experience showed loss of silicone fluid from the tissues, exposure of injected materials, infection and slippage.⁹³ These authors found that an abnormal consistency in relation to surrounding tissues is to be expected.⁹⁴ Local reactions such as firmness, tenderness and contour irregularities were reported in response to silicone injections. After 10 years of patient use, Edgerton and Wells described these same problems, and added, ominously, that complete removal was impossible.⁹⁵

Local tissue reactions to injected silicone fluid took on particular significance when the tissue involved was the breast. The deleterious effects of silicone injections in the breast were common knowledge among plastic surgeons in the 1960's. Of particular concern was the inability to distinguish large foreign body granulomatous lesions resulting from silicone injections from breast cancers. Physical examination could not discriminate

~ T. Rees, J. Platt and D. Ballantyne, An investigation of cutaneous response to dimethylpolysiloxane (silicone liquid) in animals and humans - a preliminary report, *Plast. Reconstr. Surg.* 35:13 1, 1965.

~ T. Rees, D. Ballantyne, I. Seidman, et al., Visceral response to subcutaneous intraperitoneal injections of silicone in mice, *Plast. Reconstr. Surg.* 39:402, 1967.

⁹² See T. Rees, D. Ballantyne and G. Hawthorne, Silicone fluid research: a follow-up summary, *Plast. Reconstr. Surg.* 46:50, 1970, for an overview.

~ J. Barrett Brown, M. Fryer and D. Ohlwiler, Study and use

~ *Ibid.*, p. 271.

~ M. Edgerton and J. Wells, 'indications for and pitfalls of soft tissue augmentation with liquid silicone, *Plast. Reconstr. Surg.* 58:157, 1976.

between benign and malignant masses, and mammography was useless. Breasts injected with silicone were often full of firm nodules, or firm painful nodules – either situation one where breast cancer could go undetected. Treatment of the symptomatic multinodular injected breast often involved subcutaneous mastectomy or total mastectomy.⁹⁶ Ashley and co-workers stated that the use of injectable silicone in the breast was excluded when the FDA granted permission to begin limited clinical trials.⁹⁷

C. Early FDA regulation of silicone fluid

There are so many pitfalls and challenges that it is best to remember that the body actually doesn't prefer to retain foreign bodies.

– J. Barrett-Brown, M. Fryer and D. Ohlwiler⁹⁸

Based on the work of the committee of experts, in reviewing and generating the necessary data, Dow Corning filed its Notice of Claimed Investigational Exception for a New Drug in 1965. ND #2707 was assigned in July of 1965 to permit limited Phase II trials for silicone injections.¹⁰⁰ Seven investigators were included in the original group. At approximately the same time, the FDA's attention turned to the widespread abuse of silicone fluid. In 1964, after silicone fluid had been designated a new drug, supplies of the product were seized en route to various practitioners, including Dr. Kagan. Criminal charges were brought against Dow Corning and against A. W. Rhodes, director of the medical products division for shipping an unapproved drug in interstate commerce;

⁹⁶ A series of these patients is presented in R. Parsons and H. Thering, Management of the silicone injected breast, *Plast. Reconstr. Surg.* 60:534, 1977. These problems were recognized much earlier in the literature, however. See Khoo Boo-Chai, The complications of augmentation mammoplasty by silicone Injection, *Br. J. Plast. Surg.* 27:281, 1968. See also F. Ortis-Monasterio and I. Trigos, *op. cit.*, and R. Kaden, *op. cit.*

⁹⁷ F. Ashley, et al., The present status ..., *op. cit.*, p. 415.

⁹⁸ J. Barrett Brown, M. Fryer and D. Ohlwiler, Study and use of synthetic materials such as silicone and teflon as subcutaneous prostheses, *Plast. Reconstr. Surg.* 26:263, 1960, p. 273.

⁹⁹ S. Braley, The status

¹⁰⁰ M. Lappe, testimony at Hearings ..., p. 203.

indictments were obtained in 1967.¹⁰¹ The case was resolved in 1971 when both defendants pleaded *nob contendere* and were fined \$5000 and \$1000, respectively.

As concerns about the safety of silicone injections continued to accumulate in the medical literature, the FDA suspended ND #2702 in October, 1967, citing inadequate information about manufacturing and sterilizing procedures.¹⁰² The ND was reinstated in March of 1969 after review of more extensive data about good manufacturing practices.¹⁰³ Problems with experimental design persisted, however. In 1975, Dow Corning filed NDA #17-767 with the FDA only to suspend the application in March, 1976, because supporting animal studies and human studies were again considered inadequate.¹⁰⁴ Correspondence between Dow and Margaret Clark, Acting Director, Division of Surgical-Dental Drug products, cited the data produced in the IDE trials: the study, initiated in 1965, was a non-blinded, single-treatment prospective study conducted by seven plastic surgeons and one dermatologist involving 1,333 patients.¹⁰⁵ Of these patients, 709 were treated by the dermatologist for such conditions as wrinkles and acne scars. 487 of these 709 patients did not complete their course of treatment; only 408 of the dermatologist's patients were followed sufficiently to allow any data to be collected. In addition to this deficiency, Dow Corning recognized that there was a considerable degree of treatment variation among the

¹⁰¹ Charge by grand jury, E. Dist. Mich. August 16, 1967, on a sixteen count indictment, violating Federal Food, Drug and Cosmetics Act (Title 21 USC, § 310-392) relating to 8 shipment of product designated Dow Corning Medical Fluid 360. Counts include unlawful shipment of new drug w/o complying w/statutory requirements, and shipment of drug which is misbranded. Nov. 1971 FDA Papers 5:40, November, 1971; FDA Papers 5:29, May, 1971.

¹⁰² Silicone's new role is not so prominent, Medical World News, June 6, 1969, p. 19.

¹⁰³ This regulatory history was obtained from testimony during the Hearings before the Human Resources and Intergovernmental Relations Subcommittee of the Committee on Government Operations, June 11, 1991.

~ Much of this research is summarized and referenced in T. Rees et al., Silicone fluid research

~ Letter dated 5/8/75 from J. Radrius, Food and Drug Counsel at Dow Corning, to Margaret Clark, M.D., regarding IND 2702.

five physician groupings used in the analysis. 106 After an exchange of correspondence with the FDA in 1976, Dow Corning withdrew the NDA and deferred their attempt to gain approval.

III. Silicone fluid: Years of Decline (1976-1992)

A. Public awareness

... *Celia Anderson ... sued her doctor after her face developed large sores that could not heal because of the silicone in her tissue.*

– P. Hiltz, 1992¹⁰⁷

It is becoming clear that silicone is not biologically or chemically inactive

–T. Sergott et al., 1986¹⁰⁸

In the public mind, the tide was turning against silicone fluid. Forget about silicone injections, Dr. George Thosteson advised in his medical column in the Boston Herald Traveler.¹⁰⁹ The Los Angeles Times wrote at length about an article in the Journal of the American Medical Association that provided the first hard data of adverse systemic effects in humans.⁰ Awareness was increasing in the general public that silicone injections could be harmful. Dr. Norling informed readers of the Orange County Bulletin that [i]njected silicone ... has caused two deaths and one case of temporary blindness.¹¹ 1 In describing the complications of silicone, he also observes that [w]e do not know if the

~ Ibid., p. 4.

¹⁰⁷ P. Hiltz, Doctors continue to inject silicone despite FDA warnings, agency says, New York Times, Feb. 2, 1992.

¹⁰⁸ T. Sergott, J. Limoli, C. Baldwin and D. Laub, Human adjuvant disease, possible autoimmune disease after silicone implantation, Plast. Reconstr. Surg. 78:104, 1986.

~ G. Thosteson, Her figure lacks firmness; silicone injections not the answer, Boston Herald Traveler, Jan. 9, 1969.

¹¹⁰ H. Nelson, Silicone injections a health hazard, study indicates, Los Angeles Times, Nov. 2, 1975.

E. Norling, Cleopatra's needle.

estimated 20% of silicone which leaves the site of injection goes to the liver, kidneys, lungs or other organs. The metabolism of injected silicone and method of excretion, if any, continues to remain a mystery.¹¹²

Political attention became directed toward the problems resulting from silicone injections. By 1975, there was sufficient concern in Nevada about the health risks to entertainers injected with silicone that a state law was passed criminalizing silicone injections.

Dr. Edward Kopf, a Las Vegas plastic surgeon, was responsible for bringing the dangers

of silicone injections to the attention of the Nevada Attorney General. Thousands of these women started hollering, Dr. Kopf recalled, leading him to undertake his lobbying efforts to get legislation passed.¹¹³ California and Colorado followed shortly thereafter.⁴ Doctors were prosecuted for violating these statutes and criminal convictions resulted.⁵

Successful lawsuits, with causes of actions ranging from malpractice to fraud, were brought against doctors who performed silicone injections.¹¹⁶ A charge of murder by malpractice in 1979 was dismissed due to insufficient evidence: autopsy findings of silicone in the victim's lungs following breast injection did not prove proximate causation in the court's opinion.¹¹⁷ The autopsy findings in this case bore striking similarity to those found in a 1973 Georgia criminal investigation, where silicone fluid was retrieved at autopsy from the lungs, liver, kidney, blood and brain of a woman who died of acute

¹¹² Ibid.

¹¹³ J. Foreman, Women and silicone

~ Nev. Rev. Stat. Ann. Tit. 15 @ 202.248 (1995); Cal. Bus. and Prof. Code Div. 2, Ch. 5, Art. 12 @ 2251 (1996).

~ Nelson v. Gault, 125 Cal. App. 3d 623 (1981) at 639 (describing the conviction of Dr. Gault for illegal silicone injections in 1968 under former Cal. Health and Safety Code section 26288).

¹¹⁶ Short v. Downs, 537 P.2d 754, 1975.

¹¹⁷ Lockhart v. State, Texas Ct. of Crim. Appeals, Slip op. no. 60,216, Mar. 21, 1979.

pulmonary edema following silicone fluid breast injection.¹¹⁸ The senior toxicologist in the Georgia Crime Lab, June Jones, contacted Dow Corning in 1973 to obtain specimens of Dow 200 fluid, to be compared to the silicone fluid recovered from the breasts of the victim.¹¹⁹ A particularly notorious case received widespread publicity several years later, when a male-to-female transsexual died as a result of silicone fluid injections.¹²⁰

B. Medical awareness

As far as the future is concerned, we must remember that these reports will not go away if we ignore or deny them.

– T. Sergott, et al., 1986¹²¹

As early as 1975, questions were raised in the English literature about serious systemic consequences of silicone fluid injection. Ellenbogen et al. described four patients whose complications included granulomatous hepatitis and death.¹²² The mechanism postulated for the patient's death was silicone embolization to the lungs, resulting in acute pulmonary edema. The silicone fluid injected in the victim's breasts had made its way into the vascular system and was distributed to the lungs; a similar mechanism would account for distribution of the fluid to the liver, with resulting granulomas and subsequent hepatitis. Intravascular distribution of injected silicone was similarly thought to be responsible for pneumonitis and systemic malaise following breast injection in a male-to-female

~ E. Solomons and J. Jones, J. Forensic Sciences, 1974, 191-198, The determination of polydimethylsiloxane (silicone oil) in biological materials: a case report. This article looked at the autopsy findings of a woman who died of pulmonary edema soon after the injection of silicone fluid into both breasts. At autopsy, silicone fluid was recovered from lungs, liver, kidney, brain and blood. It was concluded that the cause of death was pulmonary insufficiency secondary to a foreign substance, silicone fluid.

¹¹⁹ Proprietary Dow Corning documents, dated 4/5/73 and 4/9/73.

¹²⁰ People v. Ellison, 426 N.E.2d 1058, 1981.

¹²¹ T. Sergott, J. Limoli, C. Baldwin and D. Laub, Human adjuvant disease, possible autoimmune disease after silicone implantation, Plast. Reconstr. Surg. 78:104, 1986.

¹²² R. Ellenbogen, R. Ellenbogen and L. Rubin, Injectable fluid silicone therapy: human morbidity and mortality, JAMA 234:308, 1975.

transsexual.¹²³ All these syndromes were initially considered simple embolic reactions:

foreign material gains access to the bloodstream and is distributed to organs like the liver and the lung, where the foreign substance causes local reactions.

Similar reactions in tissues are found when natural substances like fat or small blood clots gain access to the microcirculation. These silicone-related conditions have therefore been analogized to the more familiar situation of fat embolization. However, a similar systemic illness with pulmonary manifestations was reported in a woman following silicone gel breast implantation.¹²⁴ In this case, there was no evidence for intravascular dissemination of foreign material. The question of an immunologically mediated mechanism was posed.

The possibility of an immune response to silicone injections producing illness was first raised in the Japanese literature. A 1963 report described a systemic illnesses resembling human rheumatoid arthritis following paraffin injections in the breast.¹²⁵ These authors termed the syndrome they observed human adjuvant disease, characterized by autoimmune-like symptoms, foreign body granulomas and involvement of regional lymph nodes. This syndrome was analogized to the immunologically mediated condition produced in experimental animals by injecting Freund's adjuvant to induce delayed hypersensitivity.¹²⁶ Following the criteria Miyoshi et al. listed, Yoshida presented seven cases of human adjuvant disease following silicone or paraffin breast injections.¹²⁷

123 J. Chaste, F. Basset, F. Viau, et al., Acute pneumonitis after subcutaneous injections of silicone in transsexual men, *NEJM* 308:764, 1983.

124 B. Uretsky, 'Augmentation mammoplasty associated with a severe systemic illness, *Ann. Plast. Surg.* 3:445, 1983.

125 K. Miyoshi, T. Miyamura, Y. Kobayashi, et al., Hypergammaglobulinemia by prolonged adjuvanticity in man. Disorders developed after augmentation mammoplasty, *Jpn. Med. J.* 2 122:9, 1964.

126 The biology of adjuvant disease is reviewed in Y-H. Chang, C. Pearson, C. Abe, Adjuvant polyarthritis, *Arthritis Rheum.* 23:62, 1980. See also Sergott et al., Human adjuvant disease

127 K. Yoshida, Post mammoplasty disorder as an adjuvant disease of man, *Shikoku Acta Med.* 29:318, 1973.

In 1979, Kumagai et al. examined the epidemiology of rheumatological disease among Japanese patients injected with silicone fluid, concluding that the association between silicone injections and rheumatological disorders could not be due to chance.¹²⁸ By 1984, he had identified an additional 46 patients with signs and symptoms of connective tissue disease following either silicone or paraffin injection.¹²⁹ His report included cases from the Japanese literature not previously described. Fock et al. presented additional cases where autoimmune diseases developed after silicone breast injections; these authors explicitly posited a causal mechanism for the syndrome.¹³⁰

Concerns about the association between silicone and connective tissue disease remained predominately in the province of rheumatology until the early 1980's. Plastic surgeons, if they addressed the topic at all, did so with skepticism.¹³¹ After years of questioning the potential immunological effects of silicone fluid and gel, Heggers and coworkers published the first in-depth examination of this topic in the plastic surgery literature in 1983.¹³² Their analysis corresponded to the observations of F. McDowell several years earlier:

The total surface area of the foreign body exposed to the patient's reactive mechanisms would appear to be a major factor. ... [I]f one gram of silicone gel should diffuse, molecule by molecule, through the envelope of a breast prosthesis and settle into the adjacent breast tissue – in the form of millions of tiny globules only a few microns in diameter – an enormous surface area

129 Y. Kumagai, C. Abe and Y. Shiokawa, Scleroderma after cosmetic surgery, *Arthritis Rheum.* 22:532, 1979.

129 Y. Kumagai, Y. Shiokawa, T. Medsger and G. Rodnam, Clinical spectrum of connective tissue disease after cosmetic surgery, *Arthritis Rheum.* 27:1, 1984.

130 K. Fock, P. Feng, B. Tey, Autoimmune disease developing after augmentation mammoplasty: report of three cases, *J. Rheumatol.* 11:98, 1984.

131 C. Baldwin and E. Kaplan, Silicone-induced human adjuvant disease? *Ann. Plast. Surg.* 10:270, 1983.

132 J. Heggers, N. Kossovsky, R. Parsons, et al., Biocompatibility of silicone implants. *Ann. Plast. Surg.* 11: 38, 1983.

would be exposed to the patient's reactive mechanisms. The above concept fits somewhat with what has been happening.¹³³

The accumulation of data surrounding the adverse effects of silicone injections was, no doubt, dampening enthusiasm for the product among plastic surgeons. Though there still appeared to be legitimate medical uses for silicone fluid, fewer testimonials appeared in the literature extolling its virtues. More measured descriptions of its uses were published. For example, a conclusion that ... when pure medical grade fluid is utilized in small, spaced and controlled doses and in favorable doses and in favorable deformities located in favorable sites, complications are rare appeared in a 1979 plastic surgery textbook, reflecting a more cautious attitude.¹³⁴ The spectre of connective tissue disease following silicone injection only merited a passing, unreferenced, mention in this standard reference work.

C. FDA regulation of silicone fluid

Silicone injections have been considered not safe and effective for twenty years.

– Rep. Ted Weiss, 1991'

In its letter to Dow Corning in January, 1976, the FDA cited some of the problems with the data the company had submitted in its NDA #17-767 for silicone fluid: inadequate follow-up, lack of case reports and numerous patients who left the protocol and failed to complete treatment.¹³⁵ The company resubmitted an amended ND (2702) in September, 1977. Approval was recommended by the Surgical Drugs Advisory Committee in December, 1977. In March, 1978, the silicone fluid protocols were approved by the FDA under ND 2702, despite its observation that inconsistencies still plagued the supporting

¹³³ F. McDowell, Editorial: complications with silicones – what grade of silicone? how do we know it was silicone? *Plast. Reconstr. Surg.* 61:892, 1978, p. 894

– T. Rees et al., *Inorganic implants*, p. 401.

¹³⁵ Hearings ..., p. 2.

¹³⁶ Hearings p. 197.

animal studies, so the drug should not be injected in clinical situations where the benefit to risk ratio is below that proposed in the present [clinical] protocol.¹³⁷ This protocol limited use of the drug to serious facial deformities, specifically excluding cosmetic applications. Eight investigators were involved, the original seven plus an additional dermatologist, Dr. Norman Orentreich.

Following the passage of the 1976 Medical Device Amendments to the Food, Drug and Cosmetic Act, the FDA was charged with identifying certain drugs that would be reclassified as devices.¹³⁸ The FDA announced in December, 1977, that silicone injections would be subject to these transitional provisions.¹³⁹ In 1979, Dow's ND for silicone injections was transferred from the Bureau of Drugs to the Bureau of Devices.¹⁴⁰ Its protocol was renumbered as IDE L002702.

Under this protocol, patients could be enrolled only for the treatment of serious facial deformities. The details of the clinical investigation were published in the FDA Consumer, March 1979, in an article entitled New face lift not all smiles.¹⁴¹ There, it was specified that clinical investigation was permitted only for conditions like hemifacial atrophy, facial lipodystrophy, etc., all serious facial deformities. Complications of the procedure (swelling, migration, emboli, thrombosis, discoloration, skin stretching, occasional death) were spelled out. Between 1979 and 1981, 600 patients were enrolled in the protocol.

Silicone injections were able to be used under IDE L002702 while data was collected through the protocol. The status of all transitional devices was clarified in 1988:

~ Letter dated 3/13/78 from Philip Walters, acting director, Division of Surgical-Dental Drug Products, FDA, to A. Rathjen, Dow Corning Corporation.

¹³⁸ § 520(I)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 360j(1)(1).

~ 42 FR 63472 ¹⁴⁰ 45 FR 58964

¹⁴¹ Document inserted in Hearings ...

these would all be classified in Class **rn**.¹⁴² Silicone injections, though, received special attention. The agency ruled in 1988 that although this device is classified by statute as a class III device, FDA will not publish a final classification regulation describing the device's statutory classification into class III unless the agency approves an application for premarket approval for this device.¹⁴³ Dow Corning began to gather its data for submitting a PMA application. Before the PMA application was submitted, the FDA requested from the company an interim report. The information required by this order included an update on the protocol and a summary of current information from the scientific literature. Notably, new literature was sparse to support the safety and efficacy of silicone injections.¹⁴⁴

Dow Corning filed its report on the silicone injection protocol with supporting information on August 24, 1990, as requested by the FDA. The submitted material was deemed unsatisfactory. In his review dated September 10, 1990, P. Tilton described the inadequacies of the study material: there was no follow-up longer than four years on any study patient, there were insufficient pre- and post-treatment lab studies, there were no objective measurements of improvements and there were not enough After pictures to show the individual patient results.¹⁴⁵ There is no evidence that Dow Corning sought to correct these deficiencies. Once the supporting materials had been rejected by the FDA during the preliminary evaluation, Dow Corning did not elect to pursue a formal PMA application. When the FDA required in November, 1991, that all transitional Class III

¹⁴² 53 FR 23856.

¹⁴³ Ibid.

In the 1980's, the plastic surgery community turned its attention increasingly towards silicone breast implants. The published literature available to Dow Corning about silicone injections in 1990 was not much greater than that available in 1979; this literature has been already referenced in the notes supra.

¹⁴⁵ Letter dated Sept. 21, 1990, from P. Tilton to A. Rathjen, Dow Corning.

devices submit safety and efficacy information within 60 days, Dow Corning did not respond.'

The company's attention, following the November, 1991 hearings on breast implants, was understandably directed elsewhere. It is likely that corporate attention had been focused on breast implants for several years preceding these hearings.¹⁴⁷ The IDE for silicone injections therefore became invalid in January, 1992. This product, so full of promise and problems, was allowed to retire quietly from clinical medicine.

D. FDA enforcement

In no uncertain terms let me say to the medical community that we will subject not only the manufacturers, but all those involved in the manufacturer's promotion, to the full force of the law

—Commissioner David Kessler, 1991¹⁴⁸

The 1992 report of the Human Affairs and Intergovernmental Affairs Subcommittee of the House Government Operations Committee criticized the inaction of the FDA in regulating silicone injections.¹⁴⁹ The ambivalence of the agency, the Subcommittee found, centered around its reluctance to interfere with the practice of medicine. The subcommittee report supported this finding by tracing the history of FDA enforcement of its rulings about silicone injections.

In a May, 1981, letter, the Associate Director for Compliance of the FDA recited the statutory authority of the agency to regulate drugs, and stated that physicians could not inject silicone for soft tissue augmentation unless they are participants in an ND

¹⁴⁶ 56 FR 57960.

¹⁴⁷ Some authors point to the 1984 award of \$1.5 million in the Stern lawsuit as the beginning of the breast implant crisis. See S. Lichtenstein, A discussion of the silicone gel-filled breast implant controversy. Rev. Litig. 12:172, 1992, for an overview of the early implant lawsuits. Others cite the 1988 House Subcommittee on Human Resources and Intergovernmental Relations Hearings, where the carcinogenicity of breast implants was investigated. In any case, after the December 1990 Connie Chung program on breast implants, the high profile of the issue demanded Dow Corning's constant attention.

¹⁴⁸ D. Kessler, Hearings ..., quoted in The Gray Sheet Vol. 18, June 17, 1992.

¹⁴⁹ HR. Rep. 102-1064, Nov. 19, 1992, p. 3.

protocol.¹⁵⁰ Though she recognized that resources were limited, she supported imposing sanctions on physicians who broke the law.

During the 1970's and 1980's, the FDA pursued egregious violators. In 1984, the FDA interviewed Dr. Richard Aronsohn, a Los Angeles otolaryngologist who admitted injecting silicone but stated that his use was legal because he had purchased his supply in 1962 before the substance was regulated by the FDA.¹⁵¹ The doctor is reported to have told the FDA investigator that he could legally inject his patients with mud if he felt like it; further, since he was not involved with the Dow Corning study, he did not need to report his patients' results to anyone.¹⁵² In 1985, Walter Gundaker, FDA Director of Compliance, Center for Devices and Radiological Health, suggested that Dr. Robert Russell be investigated for selling silicone fluid to physicians; however, the FDA was unable to locate, contact or even confirm the existence of this person.¹⁵³

Dr. Norman Orentreich, originally included as an investigator when ND 2702 was reinstated in 1978, came under FDA scrutiny during the late 1970's when he refused to confine his use of injectable silicone to the serious facial deformities specified in the protocol. According to the review of the 1976 Dow Corning ND, he had treated several hundred patients with liquid silicone for cosmetic purposes without including them in the research records submitted to the FDA.¹⁵⁴ Because he failed to conform to the provisions of the IDE approved in 1978, he was dropped from the roster of investigators.¹⁵⁵ Still he maintained a robust cosmetic practice as a dermatologist in New York City, with

¹⁵⁰ Letter from Ann Holt to Glen Dorfman, quoted in H.R. Rep. 102-1064, p. 3.

¹⁵¹ Memorandum from FDA District Director, Los Angeles District, to the Director of the Investigations Branch, Sept. 12, 1984, quoted in H.R. Rep. 102-1064, p. 4.

¹⁵² Ibid.

¹⁵³ Memorandum to FDA District Director, Region II, Brooklyn, N.Y., July 26, 1984.

¹⁵⁴ Medical Officer's Review of New Drug Application, Jan. 12, 1976, p. 4,9.

¹⁵⁵ H.R. Rep. 102-1064, p. 4.

appreciative movie stars as patients.¹⁵⁶ When FDA officials warned Dr. Orentreich about his use of silicone fluid without the requisite PMA(J)E, he challenged the FDA by claiming that since he manufactured his own silicone (by purchasing industrial grade silicone legally and then purifying it with filter and sterilizer), there was no interstate commerce and thus no FDA jurisdiction. A New York Times report described Orentreich's response to the FDA warning: Who is the FDA? A few technicians and one or two doctors?¹⁵⁷

Dr. Orentreich's prosecution may well have been sidetracked by a FDA memo in 1984 that mentioned that Nancy Reagan was one of his silicone injection patients.¹⁵⁸ Despite this memo, the FDA's investigation continued for awhile, resulting in a call for an injunction against Orentreich in 1985; of special concern to the Walter Gundaker in the local Office of Compliance was the presence of the same impurities in his product that were found in industrial grade silicone. The investigation was kicked upstairs shortly thereafter:

a memorandum to Gundaker from the FDA headquarters placed the Orentreich injunction recommendation in permanent abeyance.¹⁵⁹ Grounds for this decision included the agency's reluctance to single out one physician when illegal use of liquid silicone was widespread, and the agency's preference that practice of medicine issues be handled on the state level. Protected by the permanent abeyance decision, Dr. Orentreich avoided FDA investigation for several years, while continuing his practices of cosmetic silicone injections.

Not until 1991 did the FDA pursue action against physicians performing silicone injections. Anonymous letters in May of 1991 alerted the agency to the activities of a dermatologist in Several months after the FDA was asked about compliance issues at the

¹⁵⁶ Personal communication, Peter Hutt, former General Counsel FDA, Cambridge, Mass., Jan. 13, 1997.

¹⁵⁷ R. Blumenthal, New York dermatologist is fighting with FDA over silicone injections, New York Times July 19, 1991.

¹⁵⁸ FDA memorandum from George Gerstenberg to Marvin Shumate, quoted in Hearings ..., p. 192.

¹⁵⁹ This history is detailed in H.R. Rep. 102-1064, p. 5.

June, 1991, Subcommittee Hearings on silicone injections, the agency sent warning letters to Dr. Orentreich and several other physicians. Two of these doctors, Richard Aronsohn and James Fulton, were investigated by undercover FDA agents who posed as patients or as cosmetic surgeons. Along with Dr. Ricardo Samitier-Cardet in Miami and Dr. Michael Kalman in New York, these physicians received notice from the FDA that their use of silicone liquid was illegal.¹⁶⁰ The physicians addressed by the FDA were Dr. Richard Aronsohn, Dr. James Fulton.

While Drs. Aronson and Samatier-Cardet initially claimed that they would continue to inject patients with liquid silicone, since the FDA had no jurisdiction over the practice of medicine, they both later abandoned their position. In his first letter to the FDA in January, 1992, Aronsohn told the agency the virtues of cosmetic silicone injections and remarked, To my knowledge, the FDA has no legal jurisdiction over the practice of medicine.¹⁶¹ A month later, Aronson reconsidered his stance; he offered the FDA a compromise whereby he would stop injecting new patients, but wanted to complete the work on patients whose treatments were already underway. This compromise was unacceptable to the FDA. In May of 1992, a consent decree of permanent injunction was entered against him, made final later that year. Similar consent decrees were signed in 1992 by Drs. Fulton, Orentreich and Kalman.¹⁶²

¹⁶⁰ The Gray Sheet 17(49):7-8, December 9, 1991.

¹⁶¹ J. Foulke, Two doctors ordered to stop silicone injections; cosmetic surgery technique, FDA Consumer 27 (2):27, Mar. 1993.

¹⁶² The Gray Sheet 18(44):10, November 2, 1992 and FDA Consumer 27(2):27, March, 1993.

Epilogue

A. Legal Issues

Efforts by the physician community and the FDA caused a halt to liquid silicone injections into the breast. No ethical physician would do that today.

– Norman Anderson, 1990¹⁶³

With these consent decrees it might seem that what Philip Hiltz has called the strange history of silicone has come to an end. This, though, is far from the truth. Concerns about silicone fluid are very much alive today, both for patients who have received the substance in the past through injections and for patients whose exposure may be due to their silicone gel breast implants.

A number of civil cases are currently being litigated where patients suffered ill-effects from silicone injections.¹⁶⁴ Many of these injections were illegal, since the substance was administered outside the FDA ND or IDE protocols.¹⁶⁵ While systemic illness from silicone injections is hard to prove, the causal link between the injection and the local effects is easy to make. Firm, red, tender knots within and beneath the skin can result from silicone injection, leaving deformities that can only be treated by surgical excision. The plaintiffs' claims of local damage following silicone injection in the 1994 Georgia case *Knight v. Sturm* are typical; in affirming the judgment against the doctor, the Court of Appeals focused on the fact that the injections administered between 1986 and 1988 were illegal.¹⁶⁶

A larger legal problem related to silicone fluid has to do with its presence in silicone gel, the substance used to fill breast implants. Dow's investigational concerns about

¹⁶³ N. Anderson, testimony at Hearings before the Human Resources and Intergovernmental Relations Subcommittee of the Committee on Government Operations, December 18, 1990.

¹⁶⁴ Personal communication, Frederick Ellis, Boston, Mass., Jan. 16, 1997.

¹⁶⁵ See, for example, *Phillips v. Orentreich*, 1995 U.S. Dist. Lexis (S.D.N.Y. June 9, 1995)

¹⁶⁶ *Knight v. Sturm*, 442 SE. 2d 255, 1994.

silicone fluid were eclipsed in the 1970's by their preoccupation with the fabrication of breast implants; it seemed that the problems with silicone fluid were set aside as the breast implant business grew. By the mid-1970's, Dow Corning's Medical Products Division had seen itself grow from a one million dollar business in 1965 to a thirty million dollar concern; much of that growth was due to breast implants.¹⁶⁷ When regulatory difficulties with the FDA required limiting silicone injection use to a small number of rare deformities, the potential market for the product was markedly constricted. It is understandable that Dow Corning would see a shift of energies from silicone injection research to silicone breast implants as a wise business decision. But Dow Corning, ironically, was not able to get away from silicone fluid after all. Silicone gel, as it is found in breast implants, is made up of a framework of long-chain silicone polymers whose interstices are filled with silicone fluid of varying viscosity.¹⁶⁸ Some of the fluid used is the same substance used for injection: Medical Grade 360 or its equivalent.¹⁶⁹

Two of the known complications of silicone gel breast implants are gel bleed and implant rupture.¹⁷⁰ Though controversy still rages as to the frequency and clinical significance of these phenomena, it is agreed that the extravasation of gross or minute quantities of silicone gel from the implant shell brings the gel into contact with the body.¹⁷¹ If silicone fluid is part of the gel, implant rupture allows contact between human tissues and silicone fluid. If gel bleed represents the transudation of low molecular weight particles through the selectively permeable implant shell, then this shell may act as a filter to permit

¹⁶⁷ Warrick, *Forty Years ...* p. 270.

¹⁶⁸ LeVier, et al., What is silicone.

¹⁶⁹ R. Blocksma, deposition testimony In the Matter of Silicone Breast Implants, MDL 926, Vol. I, pp.

220-221, July 27, 1994.

¹⁷⁰ M. McGrath and B. Burkhardt, The safety and efficacy

¹⁷¹ B. Silverman. L. Brown, R. Bright. et al., Reported complications of silicone gel breast implants: an epidemiological review, *Ann. mt. Med.* 124:744, 1996.

the selective migration of silicone fluid into the tissues.¹⁷² If some connection between silicone gel implants and connective tissue disease can be proven, these low molecular weight particles – similar to those that make up silicone fluid – perhaps may participate in the disease mechanism.

The intensity of the debate surrounding silicone breast implants stands in stark contrast to the lack of public attention directed towards silicone injections in recent years. Perhaps the technique has been set to one side, as possessing only historical interest despite its possible relevance to the larger problems that silicone gel involves. There are other explanations for this attitudinal inconsistency, though. The medical community lost its commitment to the silicone injection techniques, perhaps in the face of government regulation that restricted its use to rare conditions. It is possible, too, that physicians responded to the negative publicity in the popular press surrounding the techniques; physicians are not immune to the influence of the media. Why, then, did surgeons continue to rally to the defense of silicone gel breast implants, despite a storm of negative publicity? This question has not yet been resolved. Possible answers have been proposed:

Marcia Angell contends that doctors stood by breast implants because of their scientific convictions;¹⁷³ more cynical observers suggest that the lucrative nature of the breast implant business inspired the dedication of manufacturers and physicians alike to the product's cause.¹⁷⁴ In any case, by the mid-1970's, silicone breast implants superseded

¹⁷² These hypotheses are intensely debated in the scientific literature and in the courtrooms. I make no effort to resolve this debate here. For an exhaustive compilation of bibliographic material and a fairly unbiased scientific evaluation of the relevant literature, see Hall et al. v. Baxter Healthcare Corp. et al. 1996 U.S. Dist. Lexis 18960 (Or., Dec. 18, 1996), where the trial judge conducted a hearing on the defendants' motions in limine to exclude the evidence submitted by the plaintiffs' experts about adverse systemic effects of silicone gel. The judge exercised his discretion under FRE 104 to appoint technical advisors to help him determine the scientific merits of the proffered testimony.

¹⁷³ M. Angell, *Silicone Breast Implants* (New York: W.W. Norton, 1996). The subtitle of her book, *The Clash of Medical Evidence and the Law in the Breast Implant Case*, points to a siege mentality that has beset some members of the medical community who feel that the very foundations of the profession are being attacked by the forces of greed and irrationality.

¹⁷⁴ It seems fair to say that this theme is part of J. Byrne's message in Informed Consent.

breast injections as the answer to what was described as woman's eternal dream –beautiful, firm and harmoniously proportioned breasts – a dream that has inspired painting, sculpture and literature since the dawn of mankind [sic].⁷⁵ In an age where sex was seen as what sells products, silicone injections had been marginalized to the treatment of obscure and distinctly unsexy conditions.

B. Ethical issues

Those who forget the past are condemned to repeat it.

–George Santayana

The active questions that remain about the ongoing effects of silicone fluid in injection and implant patients may ultimately be answered by scientific data. Larger policy questions are raised by the behavior of those who undertook to introduce this substance into the bodies of human beings without adequate data about safety and often without informed consent. While it is easy to attack such conduct, it is better to understand. While it seems clear in retrospect why Dow Corning abandoned its clinical investigation of silicone fluid when it did, it seems less clear why the company carried out its earlier investigations the way it did.

It is easy, from the perspective of the late 1990's, to criticize all who were involved. The big corporation shirked its duty to prove its product safe for human use; doctors betrayed their patients by using them as guinea pigs in medical experimentation; the FDA failed to enforce the regulations that protected the public. But investigating the history of the times when these lapses occurred leads to the conclusion that the easy criticisms fail to do justice to sociocultural realities. The fact is that these decisions made in the 1950's and early 1960's were based on a somewhat different set of moral presuppositions than what guides such decision-making today. As Silas Braley told John Byrne,

~ ~ Lalandrie and R. Mouly, *History of mammoplasty*, p. 167.

At that time, there were no tests for implant materials. There was no protocol at the FDA. If you wanted to test a device for the FDA, how would you do it? Do you feed it to a patient? What do you do? You put it under the skin of a patient and look and see what happens. And that is what we had done in many cases -

- all of which reinforced the knowledge that these materials were satisfactory for use as far as we knew at the time and were infinitely superior to anything that was available as a substitute.'

We can derive historical lessons from these decisions in the past, but we cannot

moralize quite so easily. The 20/20 hindsight with which we criticize the participants in the silicone injection debacle fails to take account of the dramatic evolution of mores that has taken place over the past forty years. The sexism, for example, that seems to pervade the actions of Dow Corning employees and many plastic surgeons only became identified as a cultural concept in the late 1960's via the Women's Movement. There seems to be little precedent in the 1950's and early 1960's for treating women in general and women patients in particular as the equals of men.

Attitudes in medical practice of the times reinforced the inferior status of the woman patient: patients in general tended to be approached paternalistically by physicians.'⁷⁷ Not until the consumer activism of the late 1960's impelled customers to ask for more information about products and services did we see a comparable demand within the doctor-patient relationship that the patient's autonomy determine her medical destiny.'⁷⁸ It is therefore not surprising that the participants in the project saw nothing wrong with their actions. From the moral perspective of the times, exploitation of women and experimentation upon human subjects may have been business as usual.

¹⁷⁶ J. Byrne, Informed Consent. p. 47.

¹⁷⁷ See, for example, J. Katz, The Silent World of Doctor and Patient (New York: The Free Press, 1986).

An entire issue of *Theoretical Medicine* is devoted to the physician's ways of influencing patient decision making through persuasion, manipulation and coercion. See *Theor. Med* 7:104-161, 181-194, 1986.

⁷⁸ R. Faden and T. Beauchamp. A History and Theory of Informed Consent (New York: Oxford Univ. Press, 1986).

This moral relativism, however, cannot coexist with the fundamental principles that have guided medical research since the Nuremberg Trials. The Nuremberg Code of 1947 set forth informed consent of the human subject as a bedrock principle.¹⁷⁹ The importance of this norm certainly was familiar to American citizens in the 1950's who had heard the horror stories of Nazi medical experiments. Further, the fiduciary nature of the doctor-patient relationship was well understood by medical practitioners of that time.¹⁸⁰ Conflicts of interest between the physician as experimenter and the physician as therapist could be appreciated even in the 1950's within the context of well-accepted medical ethics.¹⁸¹

So to say that the behavior of those involved with silicone injections was culturally understandable dodges the moral question: was it wrong? From the perspective of medical ethics, the failure of the experimenters to accumulate adequate animal data and the lack of a rigorous program of informed consent were both moral failures. What do these failures say about the individuals who were involved in carrying out the investigations? It is tempting to point a finger at Dow Corning or at individual physicians to allocate blame. But from a review of the history, it seems that the standard of culpability was more likely negligence than recklessness, especially considering the cultural climate of the times.

Why do good people do bad things? This philosophical question has preoccupied religious and secular moralists for millennia. In this case, a close reading of the texts of the times reveals a scientific and technical optimism that suggests that participants in the silicone fluid project genuinely thought that they were doing good rather than bad. Combined with this optimism was a technological arrogance about human ability to

~ Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law, No. 10 (Washington, D.C.: GPO, 1949).

¹⁸⁰ E. Friedson has been an articulate commentator on the sociology and social ethics of the profession. See E. Friedson, Professionalism Reborn (Chicago: University Press, 1994) for a compendium of his work.

¹⁸¹ Exploring this social history exceeds the purview of this paper. See, for a lucid examination of the socioeconomical development of the profession, P. Starr, The Social Transformation of American Medicine (New York: Basic Books, 1982).

solve human problems; scientific problem-solving did not require moral scrutiny because it was good in itself.¹⁸² Only after scientists began to reflect upon the human consequences of technical progress was this hubris challenged.¹⁸³ Most philosophers recognize that culture and morality must constrain science, not the progress of science alone.¹⁸⁴

While it may be difficult to allocate blame in any moral or legal sense to the participants in the silicone injection project, we can draw some conclusions for the future. The traditional dedication of the physician to the patient is a touchstone in medical practice, even in medical experimentation. The doctor has a moral obligation to ensure to his or her own satisfaction that a treatment modality is safe and effective before recommending it. The doctor-patient relationship, though, is founded on the principle of autonomy: this requires some form of informed consent in virtually every therapeutic transaction. We have at hand a body of normative doctrines that have been applied to medical practice across time. Adhering to these principles might have prevented many of the abuses that resulted from silicone injections. Another ethical line of defense is established by the procedural formalities that protect human subjects in medical experimentation. The researcher has an obligation to adhere to these regulations in spirit as well as in letter. Such moral rigor again would have protected many of those patients injured by silicone injections.

Checks and balances have been established by law to protect the public from situations like this. The IRB system, whereby institutions receiving federal funds are required to conduct prospective and ongoing review of all biomedical research involving

¹⁸² Recall the Dow Chemical slogan in the pre-*napalm* 1960's: Better living through chemistry.

¹⁸³ See M. Polanyi, *Personal Knowledge* (New York: Oxford, 1962), for example. Here a physicist reexamines the epistemological bases of scientific objectivism after realizing the moral consequences of modern physics.

¹⁸⁴ The rules protecting patients in medical experiments emanate from philosophical principles, not scientific ones. Science is different from speech: the cure for dangerous science is not more science; rather science is to be governed by human norms of morality. The doctrine of informed consent, for example, is based upon the Kantian principle of respect for persons.

human subjects, has specific requirements.¹⁸⁵ It is likely that any research like that performed with silicone fluid would have to pass some type of IRB review. More comprehensively, the FDA has a specific mandate to require manufacturers to prove new drugs and devices safe and effective.¹⁸⁶ Though the FDA of the 1960's and 1970's may seem lax by comparison to its present activism, it ultimately did its job in driving silicone injections out of business. One can argue for a more aggressive regulatory stance if problems like those caused by silicone injections are to be avoided in the future.

The possibility of a stronger FDA is met with resistance in the medical community. Government regulation is seen as inhibiting access to important drugs and devices and increasing overall health care costs. Critics note that the FDA interferes with patient autonomy and restricts the autonomy of legitimate science.¹⁸⁷ David Kessler, in response, reiterated the principles that guide the agency:

The FDA was established as a result of social mandate. Caveat emptor never has been – and never will be – the philosophy at the FDA. Manufacturers have vested interests. Between those interests and the interests of the patients, the FDA must be the arbiter. To argue that people ought to be able to choose their own risks, that government should not intervene even in the face of inadequate information, is to impose an unrealistic burden on people when they are most vulnerable to manufacturers' assertions... 188

The history of experimentation with silicone injections shows the importance of regulation in curbing irresponsible practices. The medical use of silicone fluid demonstrates that the informal moral and social controls that serve to protect patients do not always work. This history argues for a stronger regulatory stance in these times when medicine and science alike are impacted by economic incentives that conflict with human safety.

~ Protection of human subjects, 45 CFR 46, 1983. 196 21 USCA. §360.

¹⁸⁷ M. Angell, Breast implants – protection or paternalism? *NEJM* 326:1695, 1992; 1. Fisher, The silicone controversy – when will science prevail? *NEJM* 326:1969, 1992.

~ D. Kessler. The basis of the FDA's decision on breast implants, *NEJM* 326:1713, 1992.

Silicone breast implants and their poor cousin silicone injections rank among the industrial crises – thalidomide, asbestos, Three Mile Island – that have changed the way we conduct business as usual. In a technological society, we all recognize that there is some assumption of risk. But these represent situations where the market has failed to ensure a publicly desirable level of safety, so that regulators had to become involved. Ex ante, the cry is too much regulation – stifling innovation. Ex post, we wonder, Could this tragedy have been avoided? In a society of fallible people pursuing disparate interests under conditions of uncertainty, there is always the potential for disaster. Public policy will find itself always challenged to tread the fine line between overreaching and permissiveness.

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